REMARKS

Claims 23-34 have been canceled without prejudice or disclaimer. Claims 35-51 have been added and therefore are pending in the present application. Claims 35-51 are supported throughout the specification, including the original claims. For example, the % sequence identity recited in claims 35-41 is supported by page 15, lines 28-34 of the specification.

The specification has been amended to correct obvious errors. With respect to the amendments at page 1, lines 25-30 and at page 9, lines 12-19, it is well known that CBH I hydrolyzes cellobiose from the reducing end of cellulose polymer chains and that CBH II hydrolyzes cellobiose from the non-reducing end of cellulose polymer chains. *See, e.g.*, Lynd et al., *Microbiology and Molecular Biology Reviews*, 66(3): 506-577 (2002), a copy of which is attached hereto, in particular, page 513, top of the left hand column.

It is respectfully submitted that the present amendment presents no new issues or new matter and places this case in condition for allowance. Reconsideration of the application in view of the above amendments and the following remarks is requested.

I. The Objection to Claims 23, 24, and 32

The Office objected to claims 23, 24, and 32 as encompassing non-elected subject matter and for reciting two phrases twice.

Claims 23, 24, and 32 have been canceled without prejudice or disclaimer. Furthermore, the newly presented claims are directed to the elected subject matter. Applicants therefore submit that this objection has been overcome.

II. The Rejection of Claims 23, 24 and 32 under 35 U.S.C. 101

Claims 23, 24, and 32 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. Claims 23, 24, and 32 have been canceled without prejudice or disclaimer. Therefore, this rejection is rendered moot.

III. The Rejection of Claim 32 under 35 U.S.C. 112

Claim 32 is rejected under 35 U.S.C. 112 as being indefinite. Claim 32 has been canceled without prejudice or disclaimer. Therefore, this rejection is rendered moot.

IV. The Rejection of Claim 32 under 35 U.S.C. 112

Claim 32 is rejected under 35 U.S.C. 112 as failing to comply with the written description requirement. Claim 32 has been canceled without prejudice or disclaimer. Therefore, this rejection is rendered moot.

V. The Rejection of Claims 23, 24, and 32 under 35 U.S.C. 112

Claims 23, 24, and 32 are rejected under 35 U.S.C. 112 because the specification, while being enabling for a polypeptide having cellobiohydrolase II activity and the amino acid sequence of SEQ ID NO: 2 isolated from *Chaetomiaceae thermophilus* ... does not reasonably provide enablement for any polypeptide having cellobiohydrolase II activity isolated from any source or any polypeptide encoded by any polynecloetide sequence which is 75% sequence identity to SEQ ID NO: 1 or any fragment thereof." This rejection is respectfully traversed.

It is well settled that "[t]he first paragraph of section 112 requires nothing more than objective enablement. How such a teaching is set forth, either by the use of illustrative examples or by broad terminology, is of no importance." *In re Marzocchi*, 169 U.S.P.Q. 367, 369 (C.C.P.A. 1971). Moreover, "a specification disclosure which contains a teaching of the manner and process of making and using the invention in terms which correspond in scope to those used in describing and defining the subject matter sought to be patented must be taken as in compliance with the enabling requirement of the first paragraph of section 112 unless there is reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support." *In re Marzocchi*, 169 U.S.P.Q. at 369.

"The determination of what constitutes undue experimentation in a given case requires the application of a standard of reasonableness, having due regard for the nature of the invention and the state of the art ... The test is not quantitative, since a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed to enable the determination of how to practice a desired embodiment of the invention claimed ..." *Ex parte Jackson*, 217 U.S.P.Q. 804 (Bd. Pat. App. Int'f. 1982).

Factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7)

the predictability or unpredictability of the art, and (8) the breadth of the claims. *In re Wands*, 8 U.S.P.Q.2d 1400, 1404 (Fed. Cir. 1988).

Applicants respectfully submit that the claimed polypeptides are enabled by Applicants' specification. The specification includes an extensive disclosure of the claimed polypeptides, sources for obtaining the claimed polypeptides, and methods for making and using them. For example, the specification describes thirteen polypeptides having cellobiohydrolase activity by their amino acid sequence. In addition, the specification discloses that the polypeptides may be bacterial or fungal polypeptides (see, e.g., page 20, line 29 – page 22, line 3 of the specification). Bacterial sources include *Bacillus*, *Streptomyces*, *E. coli*, and *Pseudomonas*. Fungal sources include yeast such as *Candida*, *Kluyveromyces*, *Neocallimastix*, *Pichia*, *Piromyces*, *Saccharomyces*, *Schizosaccharomyces*, and *Yarrowia*, as well as filamentous fungi such as *Acremonium*, *Aspergillus*, *Chaetomium*, *Gloeophyllum*, *Malbrancheae*, *Melanocarpus*, *Meripilus*, *Myceliophthora*, *Stilbella*, *Thielavia* and *Trichophaea*.

Furthermore, the specification contains an extensive disclosure of techniques which are well known in the art and indeed routine for persons of ordinary skill in the art for identifying other polypeptides of the present invention. Applicants describe methods for preparing and probing DNA libraries (page 18, line 30 – page 19, line 3); for isolating nucleic acids encoding the cellobiohydrolases; for determining cross-hybridization of the nucleic acids encoding cellobiohydrolases using, *e.g.*, the nucleotide sequence described at page 19, lines 15-29; for comparing the percent identity of the deduced amino acid sequences of the cellobiohydrolases using the program FASTA (page 10, line 13-21).

The specification also describes various mutagenesis techniques for producing the claimed polypeptides. For example, variants can be obtained by modifying the amino acid sequence of the polypeptide of SEQ ID NO: 2 by random mutagenesis or by site-directed mutagenesis by the insertion, deletion and/or substitution of one or more amino acids. The specification further discloses that the polypeptide of SEQ ID NO: 2 may be modified by introducing one or more conservative substitutions (see page 14, lines 27-36). As described at page 26, line 15 – page 27, line 6, the claimed polypeptides may be produced by DNA recombination (shuffling). It is well within the skill of the art to isolate and identify the claimed polypeptides using Applicants' disclosure.

The Office alleges that "While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications ..., and the positions within a protein's sequence where amino acid modifications can be made with a reasonable

expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable." This is respectfully traversed.

This contention may have been true many years ago, however, it is certainly not the case as of the effective filing date of this application. As of Applicants' filing date, the state of the art had advanced significantly and the relative skill of those in the art was high. Thus, persons of ordinary skill in the art were able to routinely produce thousands of mutants of SEQ ID NO: 2 through mutagenesis and other techniques in a short period of time. See, for example, Michael Lamsa, Nils Buchberg Jensen, and Steen Krogsgaard, *Screen Automation and Robotiocs*, in *Enzyme Functionality: Design, Engineering, and Screening*, A. Svendsen, editor, Marcel Dekker, 2003. Furthermore, at page 24, line 31 to page 25, line 7, the specification discloses how one of ordinary skill in the art could identify essential amino acids in the sequence of SEQ ID NO: 2. Thus, one of ordinary skill in the art can determine which modifications, if any, would result in a loss of the desired activity/utility.

We draw the Examiner's attention to *In re Angstadt*, 190 U.S.P.Q. 214 (C.C.P.A. 1976). In *Angstadt*, the claimed process of preparing hydroperoxides used a metal salt complex as a catalyst. The specification disclosed catalysts that worked and some that gave little or no yield of hydroperoxides. The claims were rejected for lack of enablement, specifically as requiring undue experimentation to find useful catalysts. This rejection was reversed by the CCPA.

In holding that the claims did satisfy 35 USC 112, the Court observed, 190 U.S.P.Q. at 218:

> We cannot agree with the board that appellants' disclosure is not sufficient to enable one of ordinary skill in the art to practice the invention without undue experimentation. We note that many chemical processes, and catalytic processes particularly, are unpredictable, [citation omitted] and that the scope of enablement varies inversely with the degree of unpredictability involved, [citation omitted]. That this particular process is unpredictable is demonstrated further by appellants in their specification. Appellants have disclosed forty examples; one of these examples yields no hydroperoxides in the final product. Also, appellants have expressly indicated in their specification that some of these organometallic complex catalysts 'yield *** no hydroperoxides in the final product.'
>
> Appellants have apparently not disclosed every catalyst which will work; they have apparently not disclosed every catalyst which will not work. The question, then, is whether in an unpredictable art, section 112 requires disclosure of a test with every species covered by a claim. To require such a complete disclosure would apparently necessitate a patent application or applications with 'thousands' of catalysts along with information as to whether each exhibits catalytic behavior resulting in the production of hydroperoxides. More importantly, such a

> requirement would force an inventor seeking adequate patent protection to carry out a prohibitive number of actual experiments. This would tend to discourage inventors from filing patent applications in an unpredictable area since the patent claims would have to be limited to those embodiments which are expressly disclosed. A potential infringer could readily avoid 'literal' infringement of such claims by merely finding another analogous catalyst complex which could be used in 'forming hydroperoxides.'

This admonition applies with equal force to the present application, which exemplifies thirteen cellobiohydrolases and discloses numerous Examples illustrating their use. To require more would fly in the face of the *Angstadt* holding.

The Court, 190 USPQ at 218, recognized that some experimentation might be necessary for the skilled worker to select non-exemplified catalysts for use:

> Appellants have, in effect, provided those skilled in this art with a large but finite list of transition metal salts from which to choose in preparing such a complex catalyst. Appellants have actually carried out 40 runs using various transition metal salts and hexaalkylphosphoramides. If one skilled in this art wished to make and use a transition metal salt other than those disclosed in appellants' 40 runs, he would merely read appellants' specification for directions how to make and use the catalyst complex to oxidize the alkylaromatic hydrocarbons, and could then determine whether hydroperoxides are, in fact, formed. The process discovered by appellants is not complicated, and there is no indication that special equipment or unusual reaction conditions must be provided when practicing the invention. One skilled in this art would merely have to substitute the correct mass of a transition metal salt for the transition metal salts disclosed in appellants' 40 runs. Thus, we have no basis for concluding that persons skilled in this art, armed with the specification and its 40 working examples, would not easily be able to determine which catalyst complexes within the scope of the claims work to produce hydroperoxides and which do not.

However, while some experimentation might be necessary, as long as the experimentation was not "undue experimentation," the claims would not violate 35 USC 112, *Angstadt*, Id:

> Since appellants have supplied the list of catalysts and have taught how to make and how to use them, we believe that the experimentation required to determine which catalysts will produce hydroperoxides would not be undue and certainly would not 'require ingenuity beyond that to be expected of one of ordinary skill in the art.' (Emphasis added).

As in *Angstadt*, the present application identifies thirteen cellobiohydrolases. While some experimentation might be necessary to identify other non-exemplified cellobiohydrolases,

such experimentation would require carrying out a simple process without special equipment or unusual reaction conditions, as in *Angstadt*. This experimentation, if required, "would not be undue and certainly would not 'require ingenuity beyond that expected of one of ordinary skill in the art.'" (*Angstadt*, 190 U.S.P.Q. at 218). Certainly, there is no evidence of record to the contrary.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 112. Applicants respectfully request reconsideration and withdrawal of the rejection.

VI. The Rejection of Claims 23, 24, and 32 under 35 U.S.C. 102

Claims 23, 24, and 32 are rejected under 35 U.S.C. 102(b) as being anticipated by Hayashida et al. (Appl. Environ. Microbiol., 1988, 54(6): 1523-1529). This rejection is respectfully traversed.

Hayashida et al. disclose cellobiohydrolases I and II derived from *Aspergillus ficuum*. However, Hayashida et al. do not disclose a cellobiohydrolase having an amino acid sequence of SEQ ID NO: 2 of the present application. The cellobiohydrolase having an amino acid sequence of SEQ ID NO: 2 was obtained from *Chaetomium thermopilum*.

Moreover, one skilled in the art would not expect that either cellobiohydrolase derived from *Aspergillus ficuum* would have an amino acid sequence which is at least 90% identical to the sequence of amino acids 1-477 of SEQ ID NO: 2.

A cellobiohydrolase derived from *Aspergillus ficuum* could not be found in public databases. However, several cellobiohydrolases from other *Aspergillus* species were located. Attached is an alignment of the amino acid sequence of SEQ ID NO: 2 (designated "CaT") and the other *Aspergillus* cellobiohydrolases. As shown in the alignment, the *Aspergillus* cellobiohydrolyases have amino acid sequences which are less than 70% identical to the sequence of amino acids 1-477 of SEQ ID NO: 2.

For the foregoing reasons, Applicants submit that the claims overcome this rejection under 35 U.S.C. 102. Applicants respectfully request reconsideration and withdrawal of the rejection.

VII. Conclusion

In view of the above, it is respectfully submitted that all claims are in condition for allowance. Early action to that end is respectfully requested. The Examiner is hereby invited to contact the undersigned by telephone if there are any questions concerning this amendment or application.

Respectfully submitted,

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